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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,442	03/29/2002	Tadashi Mukai	05273.0034	6933

7590 12/13/2004

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,442	MUKAI ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

James M. Spear
JAMES M. SPEAR
SUPERVISORY PATENT EXAMINER
AU 1615

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Foreign Priority Papers filed 08/16/02 and the Information Disclosure Statements (IDS) filed 07/02/02 is acknowledged.

Claims 1-8 are pending. Claims 1-8 are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maruyama *et al.* (EP 0 648 487 A1) in view of Eichel *et al.* (EP 0 391 518).

Maruyama *et al.* teach a stable dispersion of enteric coating agent for the preparation of pharmaceutical compositions comprising an enteric coating base, a plasticizer and an anionic surfactant. The enteric coating base, having an average particle size of not more than 10 μm is dispersed in water in a concentration ranging from 5 to 15% by weight. The ratio of the enteric coating agent, the plasticizer and the anionic surfactant is 100 parts by weight: 15 to 40 parts by weight: 0.1 to 10 parts by weight. The enteric coating base is preferably either hydroxypropyl methyl cellulose phthalate (HPMCP) or hydroxypropyl methyl cellulose acetate succinate (HPMCAS) and the plasticizer is preferably either triethyl citrate or triacetin (see Abstract and page 3, lines 2-20).

The solid enteric pharmaceutical preparation is provided with an enteric coating film for the purpose of protecting drugs showing low resistance to acids from the attack of the acid in the stomach, of protecting the gastric mucous membrane from the attack of the drug and the drug is dissolved after the arrival at the intestines in which the pharmaceutical preparation shows its pharmacological action (pg. 2, lines 3-7).

According to Maruyama et al., the enteric coating bases can be used alone or in combination. The particle size is preferably not more than 10 μm. The plasticizers can also be used alone or in combination. Triethyl citrate is preferred because it ensures highly stable dispersibility of the coating base in an aqueous medium (page 3, lines 21-23).

Examples of anionic surfactants used in the dispersion with the plasticizer include sodium alkyl sulfates, such as sodium lauryl sulfate and sodium dioctyl sulfosuccinate (pg. 3, lines 24-29). The dispersion of enteric coating agent obtained is used for applying an enteric coating film to solid drugs, such as tablets, granules or capsules (pg. 4, lines 11-12).

The Examples at pages 4-7 demonstrate various stable granule dispersions comprising HPMCP as the enteric coating agent. The data listed in Table 2 clearly indicates that the resulting enteric coating film hardly became soluble in the gastric juice through the addition of an anionic surfactant and that the resistance to acids of the film was substantially improved.

Maruyama *et al.* teach dispersions comprising a combination of enteric coating agents, plasticizers and anionic surfactants. Maruyama *et al.* do not teach an acid in the dispersion.

Eichel *et al.* (EP '518) teach a sustained-release pharmaceutical preparation comprising an admixture of uncoated and/or single walled coated drug and multi-units of microparticles of a multi-walled coated drug. The microparticle structure preferably has a core drug, an inner wall microencapsular enteric coating, such as a cellulose acetate phthalate, a solid *acid*, such as citric acid, adipic acid or an acidic ion exchange resin layered onto or included in the enteric layer, and an outer wall microencapsulated control coating, such as a polymethacrylic acid ester copolymer or ethyl cellulose (see Abstract).

According to Eichel *et al.*, the acid within the enteric coating or the acid layer between the enteric core and control coating impedes drug release by maintaining the enteric material at a low pH.

Suitable acids that preserve the enteric core properties include citric acid, ascorbic acid, adipic acid, ethylene diamine tetracetic acid (EDTA), lactic acid and succinic acid, or polymeric acids and acidic ion exchange resins (pg. 4, lines 21-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the acids taught by Eichel *et al.* within the coating dispersion of Maruyama

et al. because Eichel *et al.* teach that the acids function to preserve the enteric properties of the core and the acids also impede drug release by maintaining the enteric material at a low pH and similarly, Maruyama *et al.* teach stable, uniform coating dispersions comprising enteric coating bases that protect drugs showing low resistance to acids in the stomach, wherein the drug is dissolved after the arrival at the intestines wherein the pharmacological action occurs. The expected result would be an improved, stabilized and better preserved enterically-formulated coating dispersion.

With regards to the instant drug (cilostazol), the prior art does not explicitly teach cilostazol. However, no criticality is seen in the use of the instant drug, since the prior art clearly teaches coating dispersions for various suitable drugs in tablet, capsule and granular forms. Moreover, the prior art teaches 'aspirin' used as the core drug, which is an anti-platelet drug, as is cilostanzol, and thus similar effects could be obtained if one drug were substituted for the other (see EP '518, pg. 5, line 32). Therefore, the instant invention, when considered as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

H. N. Sheikh HNS.

Patent Examiner

Art Unit 1615

December 09, 2004

James M. Spear

AU 1615